Lung cancer

Lung cancer is a disease in which certain cells in the lungs become abnormal and multiply uncontrollably to form a tumor. Lung cancer may not cause signs or symptoms in its early stages. Some people with lung cancer have chest pain, frequent coughing, blood in the mucus, breathing problems, trouble swallowing or speaking, loss of appetite and weight loss, fatigue, or swelling in the face or neck. Additional symptoms can develop if the cancer spreads (metastasizes) into other tissues. Lung cancer occurs most often in adults in their sixties or seventies. Most people who develop lung cancer have a history of long-term tobacco smoking; however, the condition can occur in people who have never smoked.

Lung cancer is generally divided into two types, small cell lung cancer and non-small cell lung cancer, based on the size of the affected cells when viewed under a microscope. Non-small cell lung cancer accounts for 85 percent of lung cancer, while small cell lung cancer accounts for the remaining 15 percent.

Small cell lung cancer grows quickly and in more than half of cases the cancer has spread beyond the lung by the time the condition is diagnosed. Small cell lung cancer often metastasizes, most commonly to the liver, brain, bones, and adrenal glands (small hormone-producing glands located on top of each kidney). After diagnosis, most people with small cell lung cancer survive for about 1 year; less than seven percent survive 5 years.

Non-small cell lung cancer is divided into three main subtypes: adenocarcinoma, squamous cell carcinoma, and large cell lung carcinoma. Adenocarcinoma arises from the cells that line the small air sacs (alveoli) located throughout the lungs. Squamous cell carcinoma arises from squamous cells that line the passages leading from the windpipe (trachea) to the lungs (bronchi). Large cell carcinoma arises from epithelial cells that line the lungs. Large cell carcinoma encompasses non-small cell lung cancers that do not appear to be adenocarcinomas or squamous cell carcinomas. The 5-year survival rate for people with non-small cell lung cancer is usually between 11 and 17 percent; it can be lower or higher depending on the subtype and stage of the cancer.

Frequency

In the United States, lung cancer is the second most commonly diagnosed cancer, after breast cancer, accounting for about one-quarter of all cancer diagnoses. It is estimated that more than 222,500 people develop lung cancer each year. Approximately 6.6 percent of individuals will develop lung cancer during their lifetime. An estimated 72 to 80 percent of lung cancer cases occur in tobacco smokers. Lung cancer is the leading
cause of cancer deaths, accounting for an estimated 27 percent of all cancer deaths in
the United States.

Genetic Changes

Cancers occur when genetic mutations build up in critical genes, specifically those that
control cell growth and division (proliferation) or the repair of damaged DNA. These
changes allow cells to grow and divide uncontrollably to form a tumor. In nearly all
cases of lung cancer, these genetic changes are acquired during a person's lifetime and
are present only in certain cells in the lung. These changes, which are called somatic
mutations, are not inherited. Somatic mutations in many different genes have been
found in lung cancer cells. In rare cases, the genetic change is inherited and is present
in all the body's cells (germline mutations).

Somatic mutations in the TP53, EGFR, and KRAS genes are common in lung cancers.
The TP53 gene provides instructions for making a protein, called p53, that is located
in the nucleus of cells throughout the body, where it attaches (binds) directly to DNA.
The protein regulates cell growth and division by monitoring DNA damage. When
DNA becomes damaged, p53 helps determine whether the DNA will be repaired or
the cell will self-destruct (undergo apoptosis). The EGFR and KRAS genes each
provide instructions for making a protein that is embedded within the cell membrane.
When these proteins are turned on (activated) by binding to other molecules, signaling
pathways are triggered within cells that promote cell proliferation.

TP53 gene mutations result in the production of an altered p53 protein that cannot
bind to DNA. The altered protein cannot regulate cell proliferation effectively and
allows DNA damage to accumulate in cells. Such cells may continue to divide in an
uncontrolled way, leading to tumor growth. Mutations in the EGFR or KRAS gene lead
to the production of a protein that is constantly turned on (constitutively activated). As a
result, cells constantly receive signals to proliferate, leading to tumor formation. When
these genetic changes occur in cells in the lungs, lung cancer develops.

Mutations in many other genes have been found to recur in lung cancer cases.
Most of these genes are involved in the regulation of gene activity (expression),
cell proliferation, the process by which cells mature to carry out specific functions
(differentiation), and apoptosis.

Researchers have identified many lifestyle and environmental factors that expose
individuals to cancer-causing compounds (carcinogens) and increase the rate at which
somatic mutations occur, contributing to a person's risk of developing lung cancer. The
greatest risk factor is long-term tobacco smoking, which increases a person's risk of
developing lung cancer 25-fold. Other risk factors include exposure to air pollution,
radon, asbestos, certain metals and chemicals, or secondhand smoke; long-term use
of hormone replacement therapy for menopause; and a history of lung disease such
as tuberculosis, emphysema, or chronic bronchitis. A history of lung cancer in closely
related family members is also an important risk factor; however, because relatives with
l lung cancer are frequently smokers, it is unclear whether the increased risk is the result of genetic factors or exposure to secondhand smoke.

Inheritance Pattern

Most cases of lung cancer are not related to inherited genetic changes. These cancers are associated with somatic mutations that occur only in certain cells in the lung.

When lung cancer is related to inherited genetic changes, the cancer risk follows an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to increase a person’s chance of developing the disease. It is important to note that people inherit an increased risk of cancer, not the disease itself. Not all people who inherit mutations in these genes will develop lung cancer.

Other Names for This Condition

• cancer of bronchus
• cancer of the lung
• lung malignancies
• lung malignant tumors
• lung neoplasms
• malignant lung tumor
• malignant neoplasm of lung
• malignant tumor of lung
• pulmonary cancer
• pulmonary carcinoma
• pulmonary neoplasms
• respiratory carcinoma

Diagnosis & Management

Formal Diagnostic Criteria

• Agency for Healthcare Research and Quality: Screening for Lung Cancer
  https://www.guideline.gov/syntheses/synthesis/50489/screening-for-lung-cancer
Formal Treatment/Management Guidelines


Genetic Testing

- Genetic Testing Registry: Lung cancer

- Genetic Testing Registry: Non-small cell lung cancer

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23562183

Other Diagnosis and Management Resources

- Lung Cancer Mutation Consortium: About Mutation Testing
  http://www.golcmc.com/about-mutation-testing.html

- MedlinePlus Encyclopedia: Lung Cancer--Non-Small Cell
  https://medlineplus.gov/ency/article/007194.htm

- MedlinePlus Encyclopedia: Lung Cancer--Small Cell
  https://medlineplus.gov/ency/article/000122.htm

- National Cancer Institute: Drugs Approved for Lung Cancer
  https://www.cancer.gov/about-cancer/treatment/drugs/lung

- National Cancer Institute: Non-Small Cell Lung Cancer Treatment

- National Cancer Institute: Small Cell Lung Cancer Treatment

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html

- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
• Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
• Palliative Care
  https://medlineplus.gov/palliativecare.html
• Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

**Additional Information & Resources**

**MedlinePlus**

• Encyclopedia: Lung Cancer--Non-Small Cell
  https://medlineplus.gov/ency/article/007194.htm
• Encyclopedia: Lung Cancer--Small Cell
  https://medlineplus.gov/ency/article/000122.htm
• Health Topic: Lung Cancer
  https://medlineplus.gov/lungcancer.html

**Additional NIH Resources**

• National Cancer Institute: Lung Cancer Overview
  https://www.cancer.gov/types/lung
• National Cancer Institute: Lung Cancer Prevention
• National Institute of Environmental Health Sciences
  https://www.niehs.nih.gov/health/topics/conditions/lung-disease/index.cfm

**Educational Resources**

• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org//Tumors/LungTumOverviewID5030.html
• Cancer Research UK
  http://www.cancerresearchuk.org/about-cancer/lung-cancer
• Centers for Disease Control and Prevention
  https://www.cdc.gov/cancer/lung/
• Cleveland Clinic
  https://my.clevelandclinic.org/health/diseases/4375-lung-cancer
• Disease InfoSearch: Lung Cancer
  http://www.diseaseinfosearch.org/Lung+Cancer/4334
• Johns Hopkins Medicine
  https://www.hopkinsmedicine.org/healthlibrary/conditions/adult/respiratory_disorders/LungCancer_22,LungCancer

• MalaCards: lung cancer
  http://www.malacards.org/card/lung_cancer

• Massachusetts General Hospital
  http://www.massgeneral.org/conditions/condition.aspx?id=279

• MD Anderson Cancer Center

• Memorial Sloan Kettering Cancer Center
  https://www.mskcc.org/cancer-care/types/lung

• Merck Manual Consumer Version

• Orphanet: Small cell lung cancer
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=70573

Patient Support and Advocacy Resources

• American Cancer Society

• American Lung Association

• Bonnie J. Addario Lung Cancer Foundation
  http://www.lungcancerfoundation.org/

• Free to Breathe
  http://www.freetobreathe.org/

• Lung Cancer Alliance
  http://lungcanceralliance.org/

• Lung Cancer Foundation of America
  http://lcfamerica.org/

• Lung Cancer Research Foundation
  https://www.lungcancerresearchfoundation.org/

• lungcancer.org
  https://www.lungcancer.org/

• Lungevity
  https://www.lungevity.org/
ClinicalTrials.gov
- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22lung+cancer%22

Scientific Articles on PubMed
- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Lung+Neoplasms%5BMAJR%5D%29+AND+%28lung+cancer%5BTI%5D%29+AND+genetics%5Bmh%5D+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM
- LUNG CANCER
  http://omim.org/entry/211980

Sources for This Summary
- American Cancer Society: Cancer Facts & Figures 2017


  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24420742

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24265329

Reprinted from Genetics Home Reference: 

Reviewed: December 2017
Published: January 2, 2018

Lister Hill National Center for Biomedical Communications
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